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09/26/90 23

☒ This application has been examined ☒ Responsive to communication filed on 7-6-90 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ___ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 17-20 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-16 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 17-20 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev.9-89)

15. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

16. The declaration under 37 CFR 1.132 filed 8/7/89 is sufficient to overcome the rejection of claims based upon 35 U.S.C. 102(b).

The declaration of Dr. Brownlee has been fully considered. The points made concerning the presence of trace contamination with high molecular weight contaminats is sufficient to demonstrate that the factor IX products which derive from blood retain a contamination with presumably blood derived contaminants after initial purification. The standards for anticipation require identity of the prior art with the claimed subject matter. Since the prior art teachings show trace levels of contamination, and because applicant argues that the claims are drawn to absolutely homogeneous compositoins (e.g. with respect to the presence of blood derived contaminants), it appears that the prior art does not disclose the identical subject matter as was disclosed.

17. Claims 18 to 21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amendments to the claims raise new grounds for rejection. It is obvious that the intent of applicant is to define in his claims a factor IX protein which is allegedly distinct from the prior art factor IX proteins of the prior art. The distinction is that applicant's factor IX is expressed in a mammalian host cell as opposed to being derived from plasma. Applicant uses the phrase "recombinant DNA derived" in an attempt to convey this. "Recombinant DNA-derived", however, does not indicate that there is any distinction in the context asserted. Applicant should adopt a more precise description of the protein (e.g. the product of expression of cDNA encoding factor IX from a single allelic form). The retention of the term "or of a protein sufficiently similar thereto" negates the arguments concerning allelic variation. The plain language of the claim encompasses a product which varies in precisely the same fashion as the allelic variation which applicant argues as being so significant.

Moving on, the claim recites no parameters as to absolute purity. Applicant should indicate that the product is homogeneous, in addition to being free from contamination with plasma constituents. In other words, the factor IX

product meets the limitation of clause (2) of the claim simply by being expressed by a mammalian host cell. Introduction of a term which indicates the purity of the factor IX expression product in the context of the contaminants which derive from the expression of said factor IX is an omitted, but essential element of the claim.

Finally, the reference to possession of at least 90% of the activity of "normal human plasma" should be clarified. Applicant should introduce into this clause an explanation of "normal human plasma." Instead of reciting that the reference material is "normal human plasma", which is unqualified in terms of the human factor IX protein content in the plasma, applicant should present an absolute type of reference to activity. Activity can be compared to control plasma, or to recognized international or national units of factor IX activity. In the current form, the "at least 90%" activity language becomes meaningless due to the potential variation in unqualified "normal" human blood plasma reference material.

18. Claims 17 to 20 are rejected under 35 U.S.C. 103 as being unpatentable over Suomela et al or Osterud et al, in view of Schwinn et al.

The claims are drawn to a factor IX product of expression, and a method of its use, with the critical

limitation of "being free from contamination with plasma constituents." The declaration submitted by applicant affirms that isolation and purification of factor IX to apparent homogeniety still does not rid the factor IX isolate of trace levels of contamination with "plasma constituents." The arguments of applicant concerning the unobviousness of the product and method dependent upon the product are not persuasive.

The primary disclosures each show isolation and purification of factor IX to apparent homogeneity. There are trace amounts of unidentified, uncharacterized contaminants, which appear to be derived from plasma sources. The conclusions of the authors of the primary disclosures tends to teach against the assertions of applicant that the products, as defined by the claims, is significantly improved over these essentially homogeneous blood derived versions of factor IX. Presuming that the trace contaminants derive from blood constituents, there is a lack of direct anticipation of the factor IX claims and these disclosures.

The distinction between the claimed factor IX and the apparently homogeneous factor IX of the primary disclosures, then, is limited to the presence of trace levels of blood derived contaminants. The question, then, is whether the

absence of trace contaminants renders the factor IX expression products unobvious over these disclosures.

It is noted that applicant's arguments concerning the allelic variation in caucasians is not persuasive as a basis for alleging distinction. The claims clearly encompass factor IX proteins which vary in their amino acid sequence. The plain language of the claims encompass both forms of the allelic varients. Unless applicant limits the claims to factor IX proteins having the same sequence as native factor IX, this point will not be found persuasive.

The secondary disclosure of Schwinn et al teaches procedures for rendering factor IX solutions safe for administration to humans. This disclosure presents a full, and detailed analysis of the potential hazards associated with blood derived factor IX. More importantly, this disclosure presents to the person of ordinary skill in this art a means of eliminating the threat from the presence of blood derived contaminants. The disclosure of Schwinn et al therefore provides a means for eliminating the alleged problems of the prior art; that is the potential hazards associated with use of plasma derived factor IX.

The arguments of applicant emphasize that the expression of factor IX in a suitable host cell provides a way to eliminate the possibility of hazardous blood contaminants,

and that this distinction renders the products patentable over the factor IX products of the prior art. Applicant asserts that the absence from contamination with blood derived components, standing alone, renders the products both novel and unobvious. The apparent belief of applicant is that the higher level of purity attained, without more, is sufficient to render the factor IX products patentable. This position, however, is not persuasive in view of the prior art considered as a whole.

As noted above, the presumption underlying applicant's position that the absence of blood constituent contaminant in the recombinantly produced factor IX renders this product unobvious over the same protein isolated from plasma is that the risks associated with the blood derived factor IX are removed. What applicant has failed to address is the clearly stated position of the applicant that the equivalent product was known in the art, and directly suggested by the prior art of record. A completely safe blood derived factor IX protein having trace levels of contamination with plasma constituents represents the same invention in terms of patentabilty as a completely safe factor IX protein derived from expression of an isolated DNA sequence encoding factor IX. Novelty alone does not establish patentability. Unless applicant is prepared to show that the prior art factor IX products, according to Scwhinn et al, were unusable, which seem

unlikely given the fact that Scwhinn et al were awarded a patent for their work, the arguments regarding absolute levels of purity will not be found persuasive.

19. In the interests of fairness, this action is not being made final. This is being done to allow applicant to revise the claims in a fashion consistent with the suggestions made above.

20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kushan whose telephone number is (703) 557-3434. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 557-0664.

jpk

September 24, 1990.

M. Moskowitz

MARGARET MOSKOWITZ
SUPERVISORY
PATENT EXAMINER
ART UNIT 186